

Clarke, Patrice A

From: Kinser, Robin D.
Sent: Friday, June 21, 2002 7:41 PM
To: Rustemeier, Klaus
Cc: Solana, Rick P.; Podraza, Ken F.; Kobal, Gerd; Walk, Roger A.; Carchman, Loreen; Dempsey, Ruth; Sanders, Edward; remote Reininghaus, Wolf; Patskan, George J.; Tricker, Anthony; remote Holt, Klaus von; Schepers, Georg; King, Valerie A.; Oey, Jan; Roethig, Hans; Kinser, Robin D.
Subject: RE: re Draft protocol TES

Dear Klaus--

We remain in complete agreement about adherence to our previously described standards for method validation. I have shared with you just this week the additional data provided by Covance on their NNK metabolite method.

The draft protocol for the TES that you received did not reflect our final decision (made today at our Clinical Evaluations staff meeting) to have the NNK metabolite analyses for the TES conducted by MDS Pharma Services. The NNK metabolite analysis developed by MDS is based on LC/MS/MS, requires much less sample, and costs significantly less. It is an indirect method, measuring free NNAL and then measuring total NNAL after deconjugation with glucuronidase. In addition to a well-written summary, more detailed validation data, and a method description, the MDS validation report included a copy of every calibration curve generated, information from the autosampler log for every batch, and a copy of every chromatogram generated as part of the validation. These detailed validation reports have been reviewed by S. Feng and me and show that the method performs appropriately in terms of precision, accuracy, recovery, sensitivity, selectivity, and short term stability. Shixia is bringing with him to Germany copies of the summaries from these reports for your review.

I look forward to hearing your impression of these reports. Please keep in the mind that the MDS method was initially designed for analysis of smoker urine and does not have the LLOQ we were asking Covance to achieve (LLOQ MDS method = 50pg/mL, but current sample size = 1mL urine, so scale-up is a possibility.) Also MDS has had no access to standard glucuronide and therefore has been unable to measure deconjugation efficiency.

An email informing Covance of this decision will go out this weekend.

Best regards,
Robin

-----Original Message-----

From: King, Valerie A.
Sent: Friday, June 21, 2002 10:19 AM
To: Kinser, Robin D.
Subject: FW: re Draft protocol TES

Robin:

Please see Klaus' question below - do you know of any such documents? (If you need to see what Tony's original comments were, let me know.)

Thanks,
Valerie

-----Original Message-----

From: Rustemeier, Klaus
Sent: Friday, June 21, 2002 10:16 AM
To: Oey, Jan
Cc: Solana, Rick P.; Podraza, Ken F.; Kobal, Gerd; Walk, Roger A.; Carchman, Loreen; Dempsey, Ruth; Sanders, Edward; Reininghaus, Wolf; Patskan, George J.; Tricker, Anthony; remote Holt, Klaus von; Schepers, Georg; King, Valerie A.
Subject: RE: re Draft protocol TES

Dear Jan,

I reviewed the protocol, but I did not find anything in addition to the topics already covered by Tony's response.

I agree with Tony that we should not change our requirements concerning the validation status of the methods used. Do we have any validation documents on the new methods for NNK metabolites? If yes, would it be possible to share them with me?

Best regards
Klaus

-----Original Message-----

From: Oey, Jan
Sent: Friday, June 14, 2002 23:48
To: Solana, Rick P.; Podraza, Ken F.; Kobal, Gerd; Walk, Roger A.; Carchman, Loreen; Dempsey, Ruth; Sanders, Edward; Reininghaus, Wolf; Patskan, George J.; Tricker, Anthony; Holt, Klaus von; Rustemeier, Klaus; Schepers, Georg
Cc: Roethig, Hans; King, Valerie A.
Subject: re Draft protocol TES

Dear All,

Please review the revised draft protocol and send your comments to Valerie by Jun 21.

Thank you for your help,
Jan

<< File: Protocol 8451-Draft 2 - 14 June 2002.doc >>